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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/742,785	12/20/2000	William J. Curatolo	PC10755AJTJ	8464

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
EASTERN POINT ROAD
GROTON, CT 06340

EXAMINER	
FUBARA, BLESSING M	
ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
03/06/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

~IPGSGro@pfizer.com

Office Action Summary	Application No.	Applicant(s)	
	09/742,785	CURATOLO ET AL.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-15, 18-44, 47-72, 75-92, 95-102, 104-112, 115-122, 124-132, 135-145, 156-161 and 164
Continuation of Disposition of Claims: Claims withdrawn from consideration are 3-11, 19-24, 32-40, 48-53, 60-68, 76-81, 88-91, 96-101, 108-111, 116-121, 128-131 and 136-141

Continuation of Disposition of Claims: Claims rejected are 1,2,12-15,18,25-31,41-44,47,54-59,69-72,75,82-87,92,95,102,104-107,112,115,122,124-127,132,135,142-145, 156-161 and 164.

DETAILED ACTION

Examiner acknowledges receipt of request for extension of time, change of address, amendment and remarks, all filed 11/30/07. Claims 1, 30, 58, 86, 106 and 126 are amended. New claim 164 is added. Claims 1-15, 18-44, 47-72, 75-92, 95-102, 104-112, 115-122, 124-132, 135-145, 156-161 and 164 are pending. Claims 3-11, 19-24, 32-40, 48-53, 60-68, 76-81, 88-91, 96-101, 108-111, 116-121, 128-131 and 136-141 are withdrawn from consideration.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1, 2, 12-15, 18, 25-31, 41-44, 54-59, 69-72, 75, 82-87, 92, 95, 102, 104-107, 112, 115, 122, 124-127, 132, 135, 142-145 and 164 remain rejected under 35 U.S.C. 102(b) as being anticipated by Miyajima et al. (US 4,983,593) for reasons of record and as reiterated below.

Miyajima discloses a composition that comprises 5-(5,5-dimethyl-1,3,2-dioxaphosphorinane-2-yl)-1,4-dihydro-2,6-dimethyl-4- (3- itrophenyl)-3-pyridine carboxylic acid 2-(phenylmethyl)amino) ethyl ester P-oxide hydrochloride-thanol (NZ-105) and hydroxypropylmethylcellulose acetate succinate ("HPMCAS") and the composition can be

mixed with fillers (sugars, e.g. lactose, sucrose, etc., glycitols, e.g. mannitol, sorbitol, xylitol, etc., starches, e.g. corn starch, potato starch, wheat starch, rice starch, etc., crystalline cellulose, inorganic salts, e.g. calcium hydrogen phosphate anhydride, synthetic aluminum silicate) or disintegrants, binders, lubricants or other additives (abstract; column 2, lines 34-40; column 4, lines 16-46; and Examples 1-6). Miyajima's composition also contains urea or surface active agents (column 4, line 49) and is prepared by dissolving NZ-105 and HPMCAS in an organic solvent, removing the solvent by freeze drying, spray drying or vacuum drying (column 3, lines 55-65). NZ-105 is a drug and HPMCAS meets the limitation of the concentration-enhancing polymer since HPMCAS is one of the concentration enhancing polymers recited in the instant claims. Tablets and capsules are orally administered dosage forms,

According to paragraphs [0024], [0025] and [0026] of the published application, "solubility-improved form" is a "form of the drug which has increased solubility relative to the least soluble form of the drug known. Thus, the term implies that a less soluble form of the drug exists and is either known or has been determined, i.e., known, for example, from the scientific or patent literature, or determined by or otherwise known to the investigator. A "solubility-improved form" may consist of a **highly soluble form of the drug alone**, may be a composition comprising a **highly soluble form of the drug plus inert excipients**, or may be a composition comprising the drug in **a poorly or highly soluble form and one or more excipients which have the effect of increasing the solubility of the drug,** regardless of the length of time for which the solubility is increased. Examples of "solubility-improved forms" include but are not limited to: (1) a crystalline highly soluble form of the drug **such as a salt**; (2) a high-energy crystalline form of the drug; (3) a hydrate or solvate crystalline form of a drug; (4) an amorphous

form of a drug (for a drug that may exist as either amorphous or crystalline); (5) a mixture of the drug (amorphous or crystalline) and a solubilizing agent; or (6) a solution of the drug dissolved in an aqueous or organic liquid."

"Alternatively, the term "solubility-improved form" refers to a form of the drug alone or in a composition as is described above that, when delivered to an in vivo environment of use (such as, for example, the gastrointestinal tract of a mammal) or a physiologically relevant in vitro solution (such as phosphate buffered saline or a Model Fasted Duodenal solution described below) provides, or is capable of providing, at least temporarily, a concentration of drug that is at least 1.25-fold the equilibrium concentration of drug in the use environment."

"A solubility-improved form of a drug is one that meets at least one of the above definitions." Thus, by the definition for "solubility-improved form or a drug," the NZ-105 of Miyajima meets the limitation of "solubility-improved form of a drug."

While Miyajima does not describe HPMCAS as a concentration-enhancing polymer, the instant claims recite HPMCAS as one of the concentration enhancing polymers. Aqueous solubility of less than 1 mg/ml is a property of the drug. No specific drug is recited in the instant claims. NZ-105 is a drug that is poorly soluble in water (column 1, lines 37-58). The method claims administer the drug composition. Miyajima also administers the composition.

Response to Arguments

3. Applicant's arguments filed 11/30/07 have been fully considered but they are not persuasive.

Applicant argues:

a) that crystalline hydrochloride salts, including NZ-105, the more soluble of the crystalline hydrochloride salt and the crystalline free base "have been excluded from the claims" because the claim language of "when said drug is basic, said solubility improved form has an aqueous solubility at least 2-fold the solubility of the more soluble of the crystalline hydrochloride salt and the crystalline free base drug form," excludes those forms. b) that efonidipine is not within the scope of the claimed invention because NZ-105 does not have a solubility that is 2-fold the solubility of itself and that to argue that efonidipine is 2-fold the solubility of itself is absurd. c) that Miyajima is not a physical mixture and the Miyajima does not teach a mixture in which particles of NZ-105 and HPMCAS are mixed in particulate form.

Response:

Regarding applicant's argument a) above, the section of claim 1 that states "when said drug is basic, said solubility improved form has an aqueous solubility at least 2-fold the solubility of the more soluble of the crystalline hydrochloride salt and the crystalline free base drug form," does not exclude NZ-105 because, the phrase is a relative statement that defines the inherent properties of the broad category of drugs. It is noted that the claims have not recited any specific drug but have defined what the drug may be by its function and properties. Furthermore, the claims have been amended to select the drug from "crystalline highly soluble salt form … and an amorphous form" and NZ-105 is crystalline as acknowledged by applicant.

Regarding applicant's argument b), stating that any drug would have the recited properties is **not absurd**. It is brought to applicant's attention that the generic claims are directed to i) a drug, any drug, defined by the property of solubility improved and selected from

crystalline highly soluble salt form or a high energy crystalline soluble salt form or an amorphous form. NZ-105 is crystalline and meets the requirements for a solubility improved form because the NZ-105 is more soluble that the base efonidipine keeping in mind that the definition of at least 2-fold is relative. Thus, the hydrochloride form of efonidipine, which is the NZ-105 would have the properties or characteristics recited in the section reproduced by applicant. Applicant has neither factually shown that NZ-105 cannot have the properties recited nor has named within the claims or otherwise the drugs in solubility improved form that would have the properties recited in the claims. "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The burden is on applicant to show that the properties recited in the claims as being generic to any drug cannot be applied to NZ-105. The claims have not excluded NZ-105 or any drugs within the claims' limits and scope and bounds. Furthermore, while the claims define the invention, the invention defined by the claims cannot be other than what is disclosed and the disclosure can be used as a dictionary to understand what applicant regards as his/her invention because while limitations from the specification are not read into the claims, the claims are interpreted in light of the specification (See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant's argument appears to be saying that the claims do not represent applicant's invention as interpretable from the specification, and if that is the case, then the claims would fail to comply with 35 USC 1st and 2nd paragraphs.

Regarding c), Miyajima teaches pulverizing crystals of NZ-105 (column 1, line 61) and the composition of HPMCAS and NZ-105 can be made into granules (column 2, lines 26-29) and

Miyajima doe not teach chemical reaction between the HPMCAS and NZ-105. Therefore, Miyajima teaches particulate formulation of NZ-105 and HPMCAS and the composition is a physical mixture.

The PTO does not have laboratories where test may be conducted to show differences between compositions so that "when the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

4. Claims 1, 2, 12-15, 18, 25-31, 41-44, 54-59, 69-72, 75, 82-85 and new claim 164 remain/is rejected under 35 U.S.C. 102(b) as being anticipated by Dunn (US 4,461,759) for reasons of record and as reiterated herein below.

Dunn discloses a composition that comprises a composition that comprises verapamil and acid retardant cellulose derivative (abstract; column 3, lines 6-15) and when cellulose acetate phthalate is the acid retardant, the drug and the cellulose acetate phthalate and/or bulking or disintegrant agent are granulated (column 4, lines 30-35). Verapamil is poorly soluble in water. See also claims 8 and 9. While Dunn does not describe cellulose acetate phthalate as a concentration-enhancing polymer, the instant claims recite cellulose acetate phthalate as one of the concentration enhancing polymers. Aqueous solubility of less than mg/ml is a property of the drug. No specific drug is recited in the instant claims.

While Dunn uses the hydrochloride salt in the examples, it is noted that Dunn states that **verapamil or pharmaceutically acceptable salt** (abstract; column 3, lines 6 and 7) and thus, Dunn specifically contemplates verapamil as well as the pharmaceutically acceptable salt such as

the hydrochloride. It is also noted that the claims do not recite any specific solubility except that the claims state a relative solubility. The instant composition comprises … and the instant claims do not recite a physical mixture and the prior art does not describe a chemical interaction between the drug and the polymer where a covalent or ionic bond is formed.

Response to Arguments

5. Applicant's arguments filed 11/30/07 have been fully considered but they are not persuasive.

Applicant argues that both verapamil and verapamil hydrochloride are outside the scope of applicant's claims because the claims require that the solubility of the solubility-improved form be "at least 2-fold the solubility of the more soluble of the crystalline hydrochloride salt and the crystalline free base drug form" and that this language excludes the more soluble drug form as presented in the arguments against Miyajima.

Response:

Specifically, the claims recite no specific drugs except that the drug be "solubility-improved form," which, by applicant's guidance in the instant specification at paragraphs [0024], [0025] and [0026] of the published application, is one that consists of a **highly soluble form of the drug alone**, may be a composition comprising a **highly soluble form of the drug plus inert excipients**, or may be a composition comprising the drug in **a poorly or highly soluble form and one or more excipients which have the effect of increasing the solubility of the drug,** regardless of the length of time for which the solubility is increased. Examples of "solubility-improved forms" include but are not limited to: (1) a crystalline highly soluble form of the drug **such as a salt**; (2) a high-energy crystalline form of the drug; (3) a hydrate or solvate crystalline form of a drug; (4) an amorphous form of a drug (for a drug that may exist as either amorphous

or crystalline); (5) a mixture of the drug (amorphous or crystalline) and a solubilizing agent; or (6) a solution of the drug dissolved in an aqueous or organic liquid. "Alternatively, the term "solubility-improved form" refers to a form of the drug alone or in a composition as is described above that, when delivered to an in vivo environment of use (such as, for example, the gastrointestinal tract of a mammal) or a physiologically relevant in vitro solution (such as phosphate buffered saline or a Model Fasted Duodenal solution described below) provides, or is capable of providing, at least temporarily, a concentration of drug that is at least 1.25-fold the equilibrium concentration of drug in the use environment." Verapamil or verapamil-HCl falls within the scope of what applicant terms "solubility-improved form." If the claimed composition comprising solubility improved form of any drug and any concentration enhancing polymer has 2-fold the solubility of the more soluble form of the drug, it flows that the composition of Dunn comprising verapamil or verapamil-HCl, which fits the description of "solubility-improved form," and concentration enhancing polymer would also have the property of having at least 2 fold the solubility of the most soluble form. The PTO is not equipped with laboratories to show differences between compositions and products so that "when the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The response presented above under Miyajima is incorporated here as the response to applicant's arguments applicant's arguments under Miyajima.

6. Claims 1, 2, 12-15, 18, 25-31, 41-44, 47, 54-59, 69-72, 75, 82-87, 92, 95, 102, 104-107, 112, 115, 122, 125-127, 132, 135, 142-145 and new claim 164 remain/is rejected under 35 U.S.C. 102(b) as being anticipated by Okada et al. (US 5,496,561).

Okada discloses a controlled release pharmaceutical composition comprising crystalline form of a drug (column 3, line 32); polymer such as hydroxypropylmethylcellulose acetate succinate, hydoxypropylmethylcellulose phthalate, cellulose acetate phthalate and carboxymethylethyl cellulose (column 3, lines 36-39, column 4, lines 20-25); plasticizers such as triethyl citrate, triacetin, polyethylene glycol, castor oil, polysorbitan monooleate, glycerine fatty acid ester (column 5, lines 5-8).

The instant application claims a composition that comprises a drug in a pharmaceutically acceptable solubility-improved form and a concentration-enhancing polymer is a salt and several examples of drugs that are suitable in the instant invention are listed in the specification (page 30, line 31 to page 31 line 5, page 35, line 13 to page 36 line 26 and page 26, line 30 to page 29 line 18). In the instant application, the recitation that the composition achieves a maximum equilibrium concentration of at least 1.25 fold of a drug … is a property of the drug composition and property of a composition is not separable from the composition; and thus the composition of the prior art would inherently achieve said equilibrium concentration relative to the drug.

Instant claims 25-28, 30, 54-57 and 82 recite the property of the composition and the teaching of Okada meets the limitations of said claims; diclofenac, which is one of the drugs disclosed in Okada has analgesic, anti-inflammatory and antipyretic activities; and thus Okada meets the limitation of instant claim 29. The method of the instant claims administers the drug and the concentration-enhancing polymer and the prior art teaches administering the composition to a patient/subject in need thereof.

Response to Arguments

7. Applicant's arguments filed 11/30/07 have been fully considered but they are not persuasive.

Applicant argues that Okada does not "anticipate" because Okada does not disclose drug in a solubility improved form that is physically mixed with a concentration enhancing polymer; that applicant is allowed to be his own lexicographer and applicant has defined the composition of drug and polymer as a physical mixture, that is requiring some form of mixing action; applicant also argues that the rejection based on Okada is a picking and choosing from among many polymers and drugs so that the rejection employs impermissible hindsight.

Response:

A mixture reads on mixing a polymer with the core materials in a fluidized bed to coat the core material containing the drug does not represent chemical reaction between the polymer and the drug so that Okada teaches a physical process of mixing the polymer and the drug. Okada does not describe the formation of covalent or ionic bond between the drug and the polymer, such a bond formation would not be a physical process.

The claims do not name any specific drug so that any drug would meet the drug limitation and the properties recited in the claims are inherent to the drug. Applicant has not factually shown that the drug in Okada cannot and would not have the recited properties. Regarding physical mixture and applicant's privilege of being his own lexicographer, the examiner understands a physical mixture to be a physical mixture and not one that requires chemical process between the drug and the polymer , and this understanding is well within the broad understanding of what a physical mixture is, that is, one requiring some form of mixing

action according to applicant. Okada does not describe the formation of covalent or ionic bond between the drug and the polymer, such a bond formation would not be a physical process. The examiner agrees with applicant with respect to physical mixture.

Although, applicant is allowed to be his own lexicographer, the meaning of terms used cannot be repugnant to what is known. Hence a physical mixture cannot involve a chemical reaction. Coating a core is a physical process and also meets mixing process when the term mixing is given the broadest interpretation. Regarding applicant's argument that impermissible hindsight is employed in the rejections over Okada, it is noted that the list of polymers is finite and includes hydroxypropylmethylcellulose phthalate, hydroxypropylmethylcellulose acetate succinate, carboxymethylethyl cellulose, cellulose acetate phthalate, which is fewer in number than the list of polymers in the generic claims. Regarding the list of drugs in Okada, it is noted that the broad recitation of drug in the claims without identification or any naming of specific drugs that would have the recited properties read on the list of drugs in Okada. Okada's examples are exemplifications of specific embodiments and do not represent all the embodiments of the teachings of Okada. "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

8. Claims 1, 30, 58, 86, 126, 156-161 and 164 are rejected under 35 U.S.C. 102(e) as being anticipated by Bymaster et al. (US 6,147,072).

Bymaster discloses treating psychosis, acute mania, mild anxiety states or depression by administering to a patient in need thereof a composition that comprises a first component drug selected form olanzapine, clozapine, risperidone, sertindole, quetiapine and ziprasidone, and a

second component (abstract; column 1, lines 42-46; column 2, line 9-51; and claim 2), and the composition is formulated as tablets, chewable tablets, capsules, solutions, intranasal sprays or powders, troches, suppositories, transdermal patches and suspensions (column 10, lines 8-12) and polymers such as hydroxypropyl methylcellulose phthalate and hydroxypropyl methylcellulose acetate succinate are associated with the drug (column 10, lines 61-67).

Response to Arguments

9. Applicant's arguments filed 11/30/07 have been fully considered but they are not persuasive.

Applicant argues that Bymaster does not "anticipate because it does not disclose a physical mixture of a concentration enhancing polymer and low-solubility drug." That a dosage form in which an enteric polymer is coated around a core is not a physical mixture. That Bymaster does not specifically disclose solubility improved form.

Response:

A physical mixture is given it broadest interpretation to mean a physical mixture and Bymaster did not indicate any where that the coating process involves chemical reaction between the core and the polymer. A dosage form in which an enteric coating material such as the polymers in the generic claims coats a core is a physical mixture in the broadest sense and Bymaster has not contemplated chemical reaction between the coating material and the core. Bymaster does not have to specifically narrate that the drug is in solubility improved form so long as the drug has the properties and characteristics recited to define what a solubility improved form is.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 86, 87, 92, 95, 102, 105-107, 112, 115, 122, 124-127, 132, 135 and 142-145 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dunn (US 4,461,759).

Dunn is discussed above. Dunn discloses a composition where the drug verapamil and cellulose acetate phthalate are granulated. Dunn does not discuss administering the verapamil composition to a subject in need thereof. Verapamil is a cardiovascular drug and the drug composition has to be administered in order for it to provide cardiovascular positive effect in a subject. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the cardiovascular composition comprising verapamil. One having ordinary skill in the art would have been motivated to administer the verapamil

formulation to a subject in need thereof with the expectation of treating cardiovascular problems such as irregular heartbeats (arrhythmias) and high blood pressure.

Response to Arguments

13. Applicant's arguments filed 11/30/07 have been fully considered but they are not persuasive.

Applicant argues that the verapamil and verapamil hydrochloride of Dunn are outside the scope of claim 86 according to what has been set forth regarding the exclusion of Verapamil in applicant's invention in the preceding sections; that Dunn is concerned with solving different problem from applicant because Dunn seeks to retard release of verapamil instead of enhancing the concentration.

Response:

The examiner thanks applicant for recognizing the typographical error of omitting claim 86. Regarding applicant's argument that Verapamil is excluded in the claimed invention, it is noted that the claims are not specific to any specific drug and as described above under Dunn, the broad recitation of any drug having the recited properties does not exclude verapamil. Applicant recognizes on page 5 of the remarks that the drug forms of Dunn are verapamil and verapamil pharmaceutically acceptable salt. Thus, by applicant's own admission, Dunn is concerned with verapamil. The claims are directed to composition containing a drug, any drug, in a solubility enhanced or improved form; a drug having an aqueous solubility of less than 1 mg/ml is not in the solubility enhanced form but that the solubility enhanced form is at least 2-fold the solubility of the more soluble of the drug form. Therefore the drug in the claimed composition is not in the form that has a solubility of less than 1 mg/ml. The claims are not directed to method of enhancing the concentration of drug, rather, the claims are directed to

composition comprising solubility-improved from which according to applicant encompasses **highly soluble form of the drug alone or** a crystalline highly soluble form of the drug **such as a salt (**see paragraphs [0024], [0025] and [0026] of the published application). Therefore, verapamil hydrochloride is a solubility-improved form falling within the scope of applicant's solubility-improved form as per paragraphs [0024], [0025] and [0026] of the published application.

No claim is allowed.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-272-0594.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Blessing M. Fubara/
Examiner, Art Unit 1618

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618